IN THE SPECIFICATION

Please amend the paragraph at page 4, lines 6-13 to read as follows:

-- Behrens et al. (2001) *Bioconjugate Chem*, 12:1021-1027 have incorporated analogs of Hoechst 33258 onto the N-terminus of a defined polypeptide backbone to yield a polypeptide-containing compound ~~the~~ **that** retains the AT-rich binding preference of the unmodified Hoechst 33258 dye. In this work, a Hoechst 33258 analog was bonded to the N-terminus of the cationic polypeptide KSPKKAKK (SEQ. ID. NO: 1). The cationic polypeptide so modified was found to bind to double-stranded DNA with approximately 10-fold higher affinity than the Hoechst analog itself, without altering the AT-rich binding preference of the unmodified Hoechst 33258 dye.--

At page 11, after the last paragraph, please insert the following new paragraph (a brief description for newly added Figs. 4a, 4b, and 4c):

-- FIG. 4a is a schematic diagram depicting the anchor moiety as circles, and the linking moiety as X. FIG. 4b is a schematic diagram depicting the positioning of the target nucleic acid, including the anchor moiety, linker, test compound and the Exd regulatory factor. FIG. 4c shows the eight linking moieties used in the Examples. --

Please amend the paragraph at page 14, lines 9-19 to read as follows:

-- The principal utility of the present invention is a method to examine the molecular basis of nucleic acid binding properties (cooperative and otherwise) displayed by regulatory factors (for example, Hox proteins and their partners). Using the method, various test compounds can be ~~be~~ used to perturb, mimic, or otherwise modulate transcriptional networks that are dictated regulatory factors. Thus, the present method is useful to help elucidate the nature of nucleic acid binding and the role of opposing regulatory functions of regulatory factors (that is, the ability of a factor to enhance or ~~initial~~ **initiate** transcription under one set of conditions, and to silence or suppress

transcription under another set of conditions). The invention also contributes toward improving the precision with which ATFs can be designed, evaluated, and utilized to trigger specific transcriptional networks *in vivo* or *in vitro*.--

Please amend the paragraph at page 16, lines 16-21 to read as follows:

-- The invention can also evaluate *in vivo* function and examine the role of opposing regulatory functions. For example, the compositions of matter described herein can be fed to ~~first instar Drosohila~~ **Drosophila** larvae**,** and their effect**s** on various developmental pathways that are influenced both by, for example Ubx and ~~Lab~~ **Exd**, can be determined. Another mode of delivery would be to microinject polyamide conjugates into embryos. In either case, the polyamides would be coupled to carrier peptides to facilitate their mobility into cells.--

Please amend the paragraph at page 17, line 27, to page 18, line 5 to read as follows:

-- The binding site to be studied in the nucleic acid target can be any regulatory factor binding site, without limitation. Exemplary binding sites that can be defined within the nucleic acid target include, without limitation, promoter binding sites, transcription factor binding sites, enhancer binding sites, silencer binding sites, suppressor binding sites, and the like. A promoter is a regulatory sequence of DNA that is involved in the binding of RNA polymerase to ~~initiated~~ **initiate** transcription of a gene. An enhancer is **a** regulatory sequence of DNA that can increase the utilization of promoters, and can function in either orientation (5'—3' or 3'—5') and in any location (upstream or downstream) relative to the promoter. A silencer sequence or suppressor sequence generally has a negative regulatory effect on expression of the gene.--

Please amend the paragraph at page 24, line 21, to page 25, line 2 to read as follows:

-- As shown in Example 7, the anchor moiety is a sequence-specific hairpin polyamide that is composed of N-methylpyrrole (Py) and N-methylimidazole (Im) hetrocycles linked via amide bonds. The test compound, also referred to as the "hook," is a conserved tetra-peptide (YPWM) (SEQ. ID. NO: 10) derived from the Hox-family of transcription factors. The Hox tetra-peptide interacts with Extradenticle (Exd)—a DNA-binding protein—and stabilizes the assembly of a ternary Hox-Exd-DNA complex. The crystal structure of the Hox-Exd-DNA complex was used to guide the design of a synthetic molecule that would present the YPWM **(SEQ. ID. NO: 10)** peptide hook adjacent to the DNA binding site and stabilize the association of Exd with DNA. The polyamide anchor moiety of the composition was conjugated to the YPWM **(SEQ. ID. NO: 10)** test compound using a propyl linker. This synthetic molecule efficiently mimics the ability of the natural Hox protein to stabilize Exd binding to DNA.--

Please amend the paragraph at page 33, lines 5-6 to read as follows:

-- FIG. 1d: Compound **3**: Lane 5-17: 1 ~~**pM**~~ **μM**, 500 nM, 200 nM, 100 nM, 50 nM, 20 nM, 10 nM, 5 nM, 2 nM, 1 nM, 500 pM, 200 pM, 100 pM, respectively.--

Please amend the paragraph at page 33, lines 22-27 to read as follows:

-- FIGS. 2a, 2b, 2c and 2d ~~**show**~~ depict the DNA duplexes used for the EMSA studies. The binding site for the Exd protein is marked by a box, the polyamide or Hox protein binding site is shown in boldface, FIG. 2a depicts the optimal template. FIG. 2b depicts a 2-bp mismatch in the Exd site. FIG. 2c depicts a 2-hp mismatch in the PA binding site. FIG. 2d depicts a composite Ubx-Exd binding site (see Passner et al. (1999) *Nature*, 397:714-719).--

Please amend the paragraph at page 33, line 28, to page 34, line 7 to read as follows:

-- Gel-shift experiments: The master mix contained 50% BSA/50% glycerol, reaction buffer (150 mM potassium glutamate, 50 mM HEPES pH 7.0, 1 mM DTT, and 5'-end labeled DNA (^{32}P). The final concentrations in the samples were 100 ng/μL BSA and 10% glycerol. Polyamides were kept in subdued lighting whenever possible. Upon addition of the polyamide to 1 pM DNA, the samples were incubated at ~~25°C~~ **25°C** for 30 minutes in a 20 μL reaction. Next, Exd was added to the samples and incubated for 1 hour at 4°C. A 9% acrylamide/3% glycerol gel was pre-run for 15 min prior to loading. In each lane 15 μL of a 20 μL reaction were loaded while the gel was running to prevent the samples from being diluted. The gels were run at 4°C/185 V. Gels were dried, exposed to a phosphorimager screen, and visualized using a Molecular Dynamics phosphorimager.--

Please amend the paragraph at page 34, line 30, to page 35, line 7 to read as follows:

-- In Examples 1-6, a structure-based design was used to generate a composition of matter comprising a polyamide anchor moiety, a glycine linker moiety, and a polypeptide test compound. As shown in the above Examples, this approach ~~that~~ demonstrates that the test compound as presented **to** the transcription factor**[[,]]** had functionality to recruit binding of the transcription factor to an isolated nucleic acid target. In the Examples, compound **2** displays a functional test compound and compound **3** displays a non-functional test compound attached to the PA-propylamine side chain via a glycine linker. As noted in the Example 3, the compounds were synthesized by solution-phase coupling of protected peptide acid fragments to the parent PA **1**.--

Please amend the paragraph at page 35, lines 8-13 to read as follows:

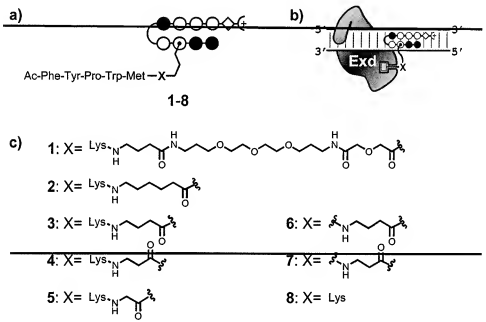
-- The DNA-binding properties of the compounds **1-3** were investigated by quantitative DNase 1 footprinting assays. The equilibrium binding constants of each of the compounds for a matched versus three single base pair mismatch sites is compiled in Table 1. The lower strand sequence is shown in the header. Mismatched base pairs are underlined. The residue under the YPWM peptide **(SEQ. ID. NO: 10)** is in bold. Relative specificities are given in square brackets.--

Please amend the paragraph at page 36, lines 14-25 to read as follows:

-- The Examples thus provide convincing evidence that: 1) the YPWM peptide **(SEQ. ID. NO: 10)** contributes significantly to the cooperative interaction between a Hox protein and its partner on a DNA target; and 2) the present method is capable of evaluating and quantifying the nature of the cooperation. In summary, the Examples demonstrate that interactions between a nucleic acid-binding protein and its corresponding nucleic acid target can be evaluated using a composition of matter comprising a suitable DNA target having conjugated thereto a minor groove binding polyamide anchor/glycine linker/peptide test compound. The ability of compound **2** to recruit Exd more efficiently than its natural Hox protein partner illustrates that structure-based modular design is a valid strategy to test and evaluate both ~~**compound**~~ **compounds** that modulate the action of artificial transcription factors, as well as a means to evaluate and test artificial transcription factors themselves.--

Please amend the paragraph at page 37, lines 3-12 to read as follows. (Note, please remove the drawing depicting Formulas (a), (b), and (c)):

-- Eight compounds were synthesized each bearing the same polyamide and the FYPWM (SEQ. ID. NO: 13) penta-peptide test compound. **FIG. 4a** ~~**Formula (a)**~~ depicts the anchor moiety as circles, and the linking moiety as X. **FIG. 4b** ~~**Formula (b)**~~ depicts the positioning of the target nucleic acid, including the anchor moiety, linker, test compound and the Exd regulatory factor. **FIG. 4c** ~~**Formula (c)**~~ shows the eight linking moieties used in this Example.



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Please amend the paragraph at page 37, line 13, to page 14, line 6 to read as follows:

-- The propyl end of the linker projects off the N-methylpyrrole of the anchor moiety in each case. This arrangement is sufficient to project the test compound over the minor groove and position it adjacent to the major groove where Exd would bind. The eight varying linkers range from ~33Å in the case of the PEG linker to ~2.5Å in the case of the lysine linker. Linkers 1-5 and 8 bear an additional lysine residue at the C-terminus of

their YPWM hook **(SEQ. ID. NO: 10)**. This residue is often seen in hooks in various Hox proteins, in our case we treat it as an additional linker residue. The lysine also improves the solubility of these rather hydrophobic compounds. Compounds 6 and 7 do not bear the lysine and are less soluble. Each of the compounds ~~were~~ **was** synthesized by solid phase methods, as described hereinabove. The polyamide was synthesized first, and then conjugated by conventional means to each of the eight linkers, which was then conjugated (by conventional means) to the peptide. Care was taken to ensure that the tyrosine residue was not racemized, and that the tryptophan was not oxidized. The compounds were confirmed by MALDI-TOF mass ~~spectrometery~~ **spectrometry** (data not shown).--

Please amend the paragraph at page 39, lines 1-15 to read as follows:

-- Electrophoretic mobility shift assays (data not shown) indicated that each of the eight compounds was able to stabilize Exd binding to the adjacent cognate DNA site (TGAT). Neither the parent polyamide lacking the YPWM hook **(SEQ. ID. NO: 10)**, nor the polyamide bearing an altered hook (FYPAAK) (SEQ. ID. NO: 14) was able to stabilize Exd binding (data not shown). The assays were performed with 50 nM of the conjugate pre-incubated with target DNA (thus to bind the anchor moiety to the target nucleic acid) followed by the addition and incubation with Exd. At 50 nM, each of the conjugates binds DNA stoichiometrically and the affinity of Exd can be readily monitored by the formation of ternary complex with increasing concentration of the conjugate. The data indicate that compounds incorporating linkers 7 and 8 (*i.e.*, short linkers (< 4Å when fully extended), do not optimally position the test compound with respect to its hydrophobic docking site on the surface of Exd. The absence of the lysine residue in linker 6 did not appreciably alter the ability of the corresponding target nucleic acid to recruit Exd in comparison to the compound using linker 5 (which does bear the lysine residue and is roughly one angstrom longer).--

Please amend the paragraph at page 39, lines 21-23 to read as follows:

-- While binding at 4°C shows a small effect of linker length on the ability of ~~compound~~ **compounds** using linkers 1-6 to recruit Exd, it was likely the entropic penalty of bearing a larger linker would be more apparent at higher temperatures.--